Integrated Model of the Eye/Optic Nerve Head Biomechanical Environment

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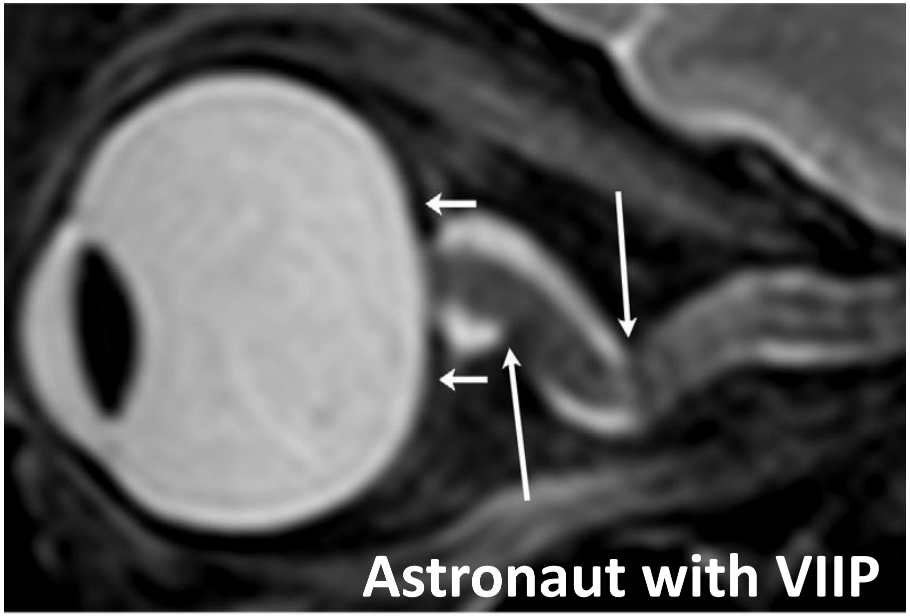
Structural Changes in the Posterior Eye



Kramer et al. Radiology, 2012.

Hypothesis

Increased CSF pressure, transmitted to the RB-SAS, drives remodeling of connective tissues in the posterior eye and optic nerve sheath

Eventually leads to the vision disturbances characteristic of VIIP

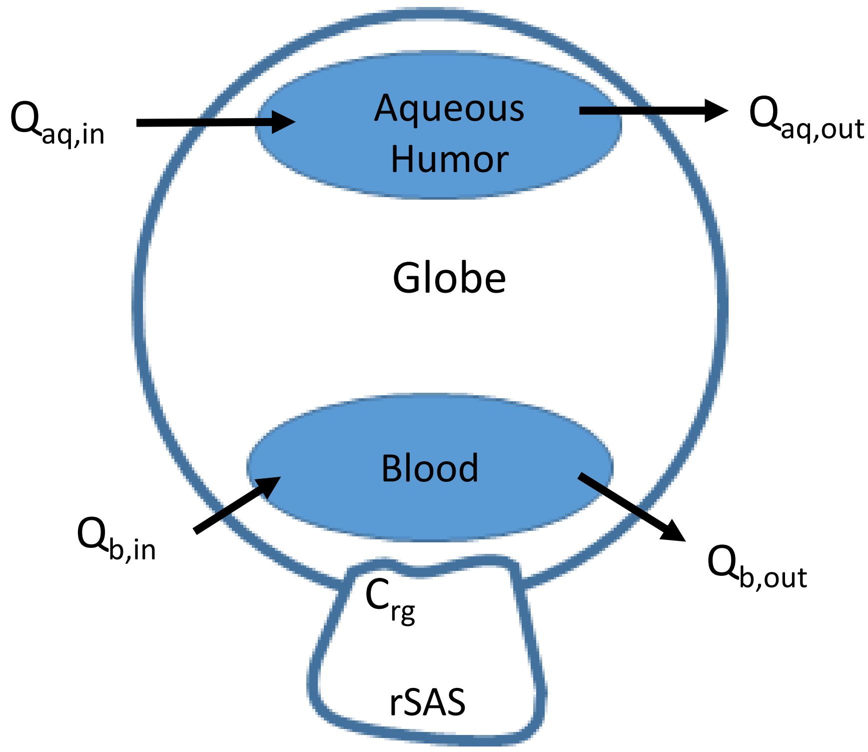
Goal

Develop an integrated model approach to understand how environmental conditions impact deformation of tissues of the posterior eye and optic nerve sheath

Key tools: Numerical and finite element modeling

Numerical Model

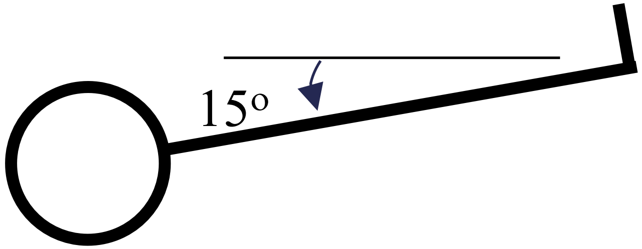
Lumped Parameter Eye Model



Model features:

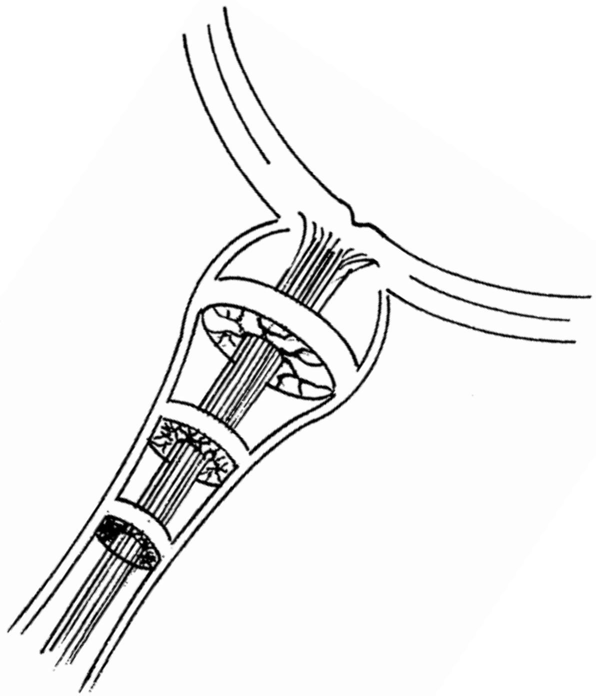
- Four-compartment model
  - Anterior Chamber
  - Blood compartment (cardiovascular model)
  - Globe
  - Retrobulbar subarachnoid space (rSAS)

Simulating Head Down Tilt (HDT)

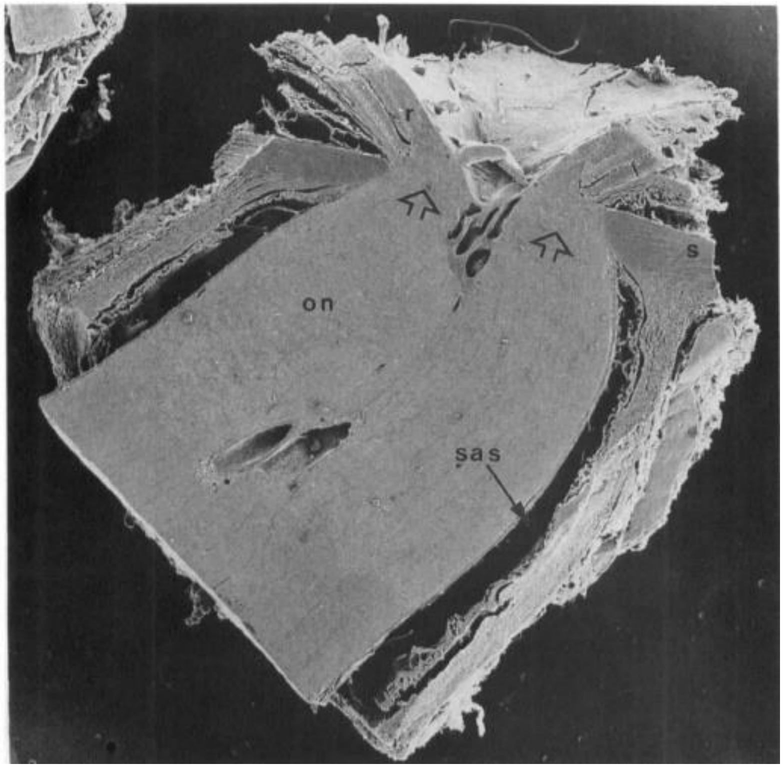


Finite Element Model

Finite Element Geometry

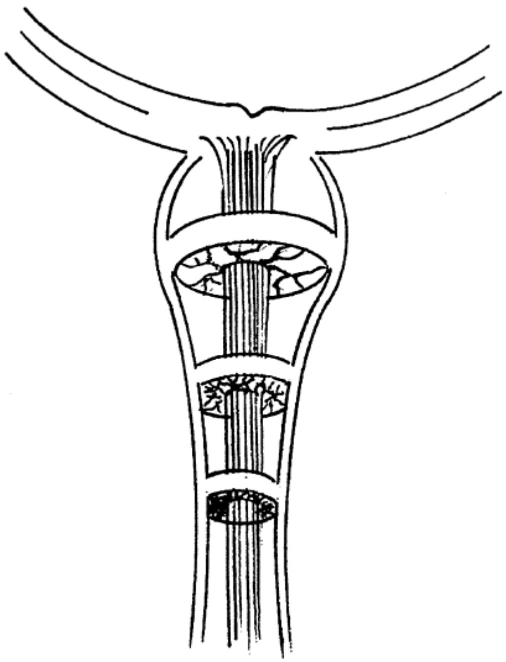


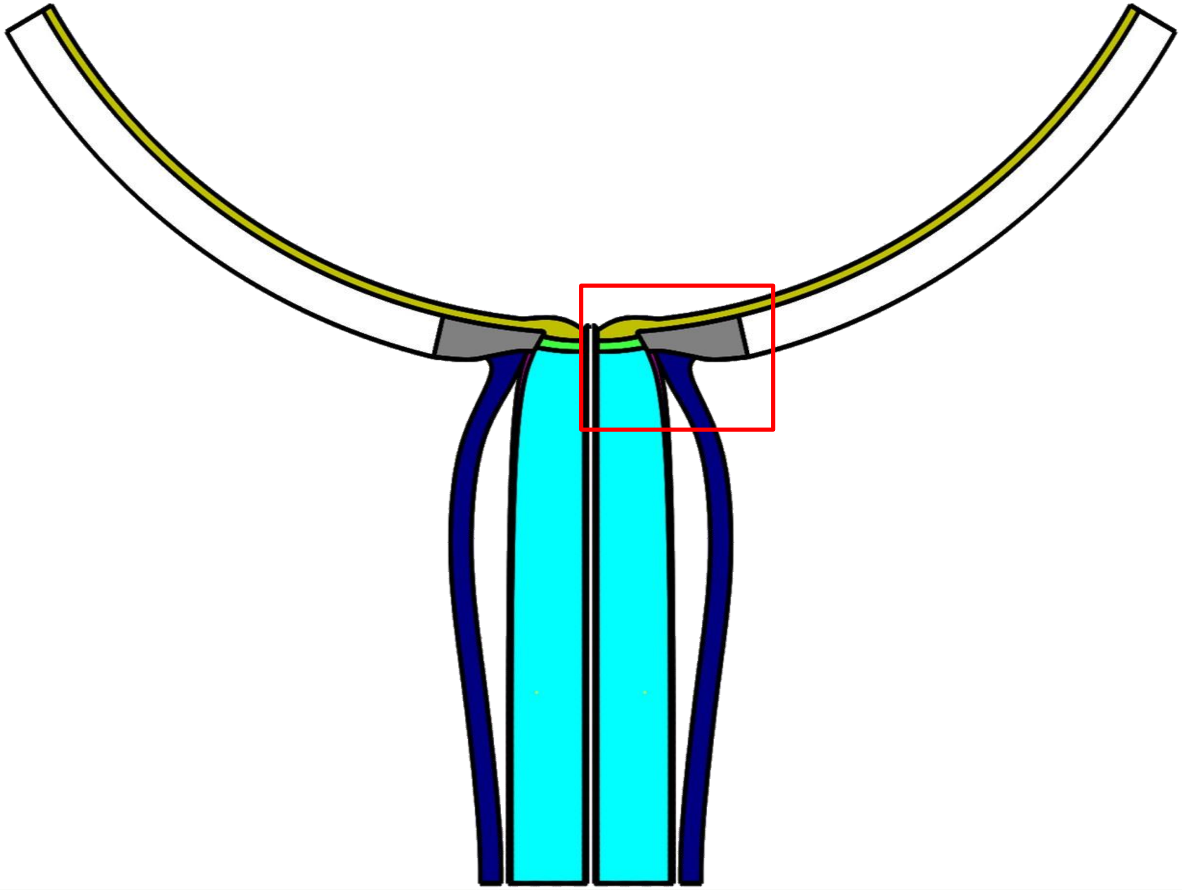
Hansen et al. Acta Ophthalmologica, 2011.



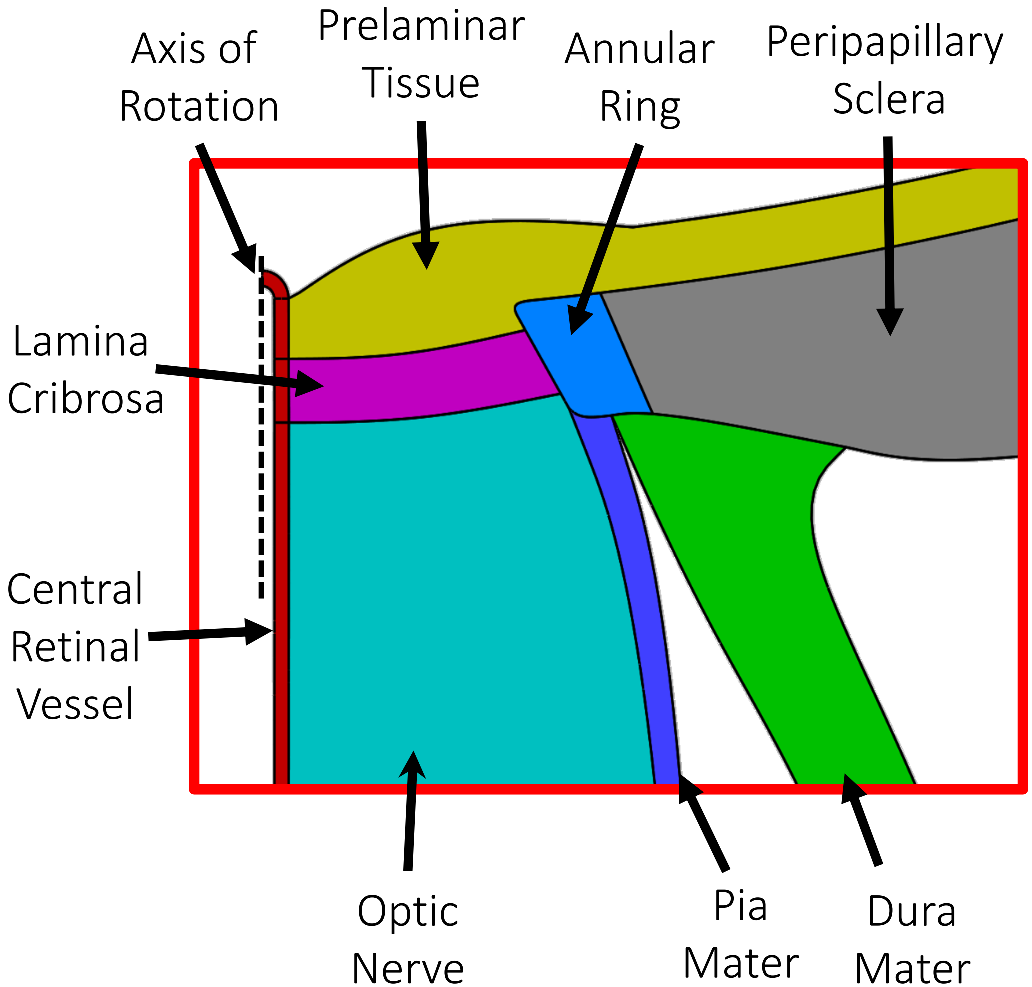
Adopted from Ekington et al. 1990

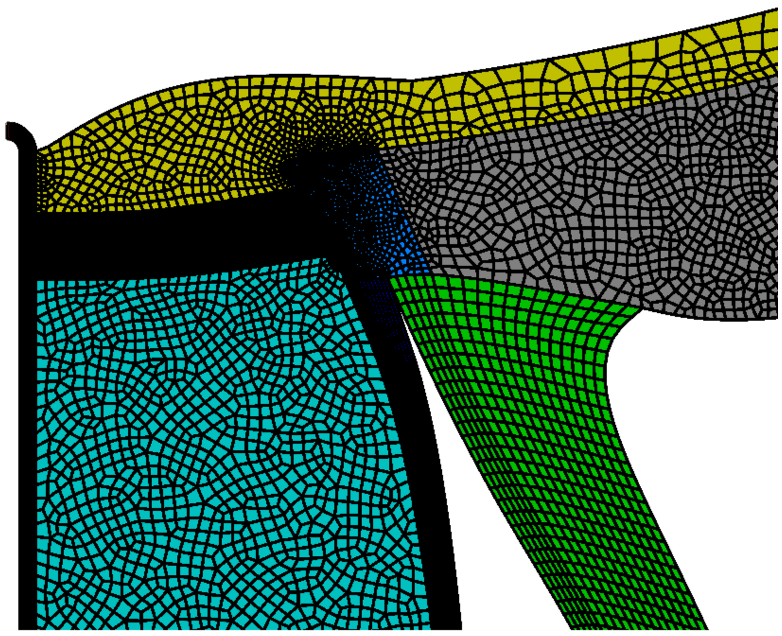
Model Overview





Finite element model





Tissue Constitutive Models

- Mooney-Rivlin plus von Mises Distributed Fibers
  - Proposed by Girard and Ethier for the the sclera
  - Implemented into FEBio V2 by Gouget and Girard for thin tissues

$$\Psi = F_1\left(\tilde{I}_1, \tilde{I}_2\right) + \int_{\theta_p - \frac{\pi}{2}}^{\theta_p + \frac{\pi}{2}} P(\theta)\, F_2\left(\tilde{\lambda}[\theta]\right) d\theta + \frac{K}{2}[\ln(J)]^2$$

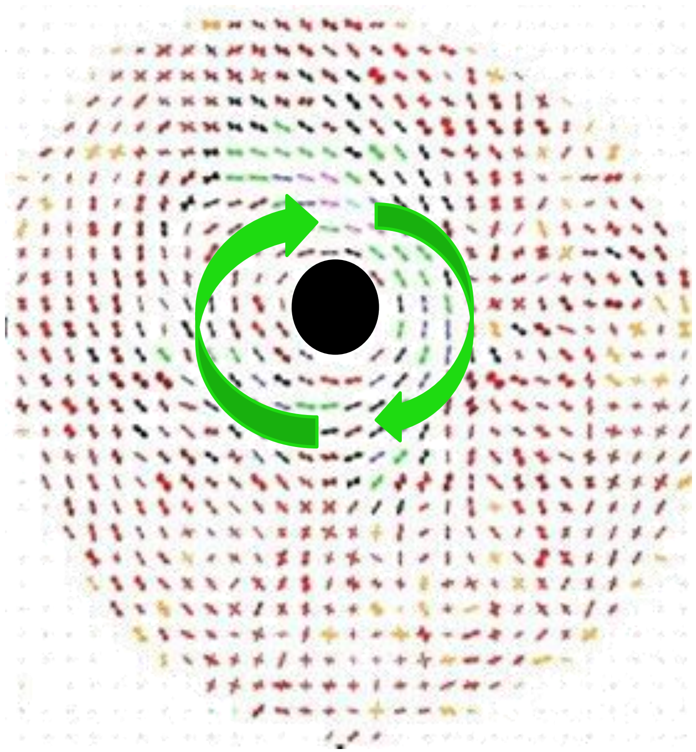
- F_1 represents ground substance (neo-Hookean): $F_1 = C_1\left(\tilde{I}_1 - 3\right)$
- F2 represents collagen fibers
  - Collagen fibers are loaded within their non-linear region

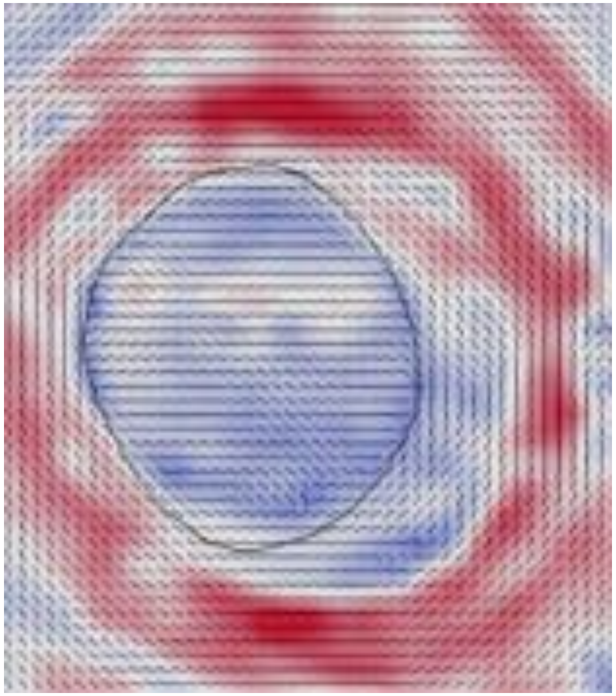
$$\check{\lambda}\frac{\partial F_2}{\partial \check{\lambda}} = 0, \check{\lambda} \leq 1$$

$$\check{\lambda}\frac{\partial F_2}{\partial \check{\lambda}} = C_3\left(e^{C_4(\lambda - 1)} - 1\right), 1 < \check{\lambda} \leq \lambda_m$$

Collagen Orientation in the Sclera

- Sclera: collagen fibers treated as transversely isotropic
- Peripapillary sclera: moderately aligned collagen fibers
- Annular ring: highly aligned collagen fibers





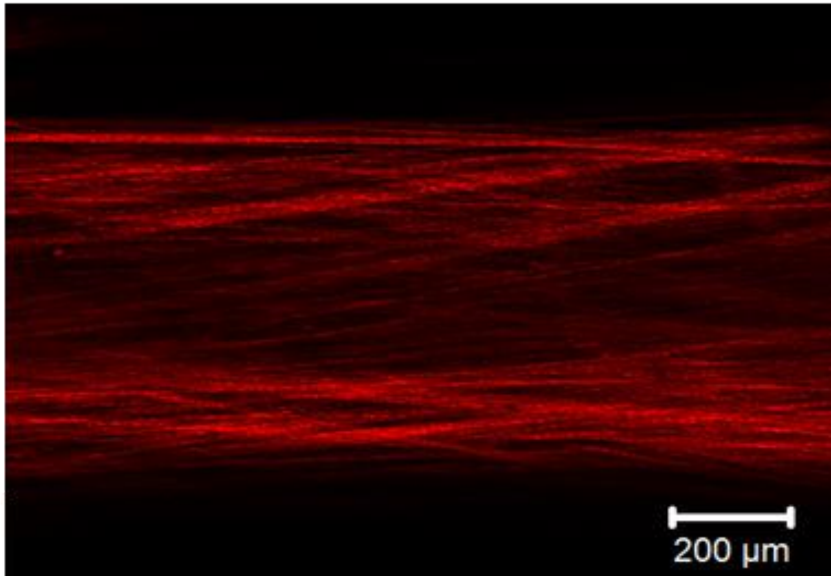
~ Pijanka et al. 2012 & Zhang et al. 2015

Collagen Orientation in the ONS

Pia mater and dura mater: fibers were modeled as transversely isotropic

~Raspanti et al. 1992 Noort et al. 1980 & Raykin et al. 2015

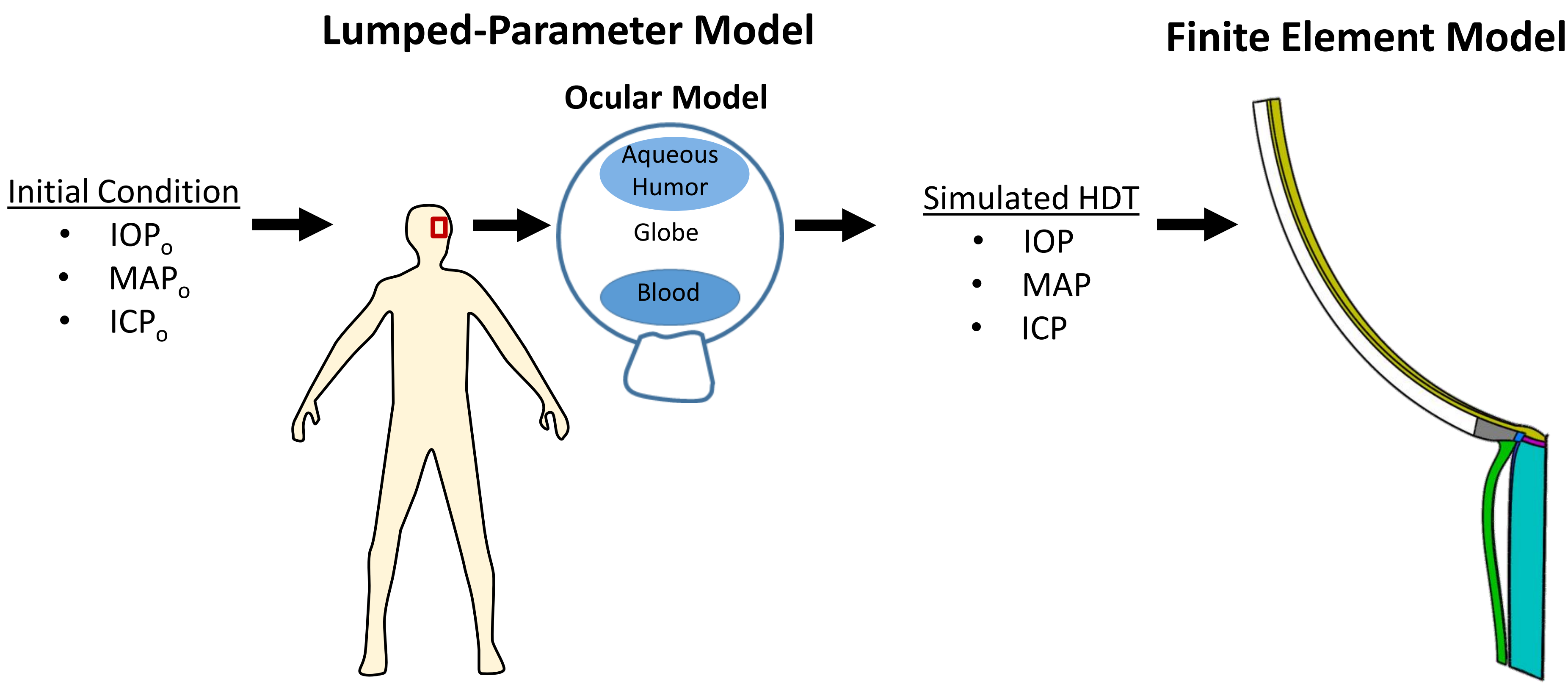
Dura Mater



Tissue Material Properties

	Mooney-Rivlin solid with embedded collagen fibers
Material Inputs	Ground Stiffness (c_1) Collagen Stiffness (c_3 & c_4)
Tissue Properties	Distribution of embedded collagen fibers

Integration Overview



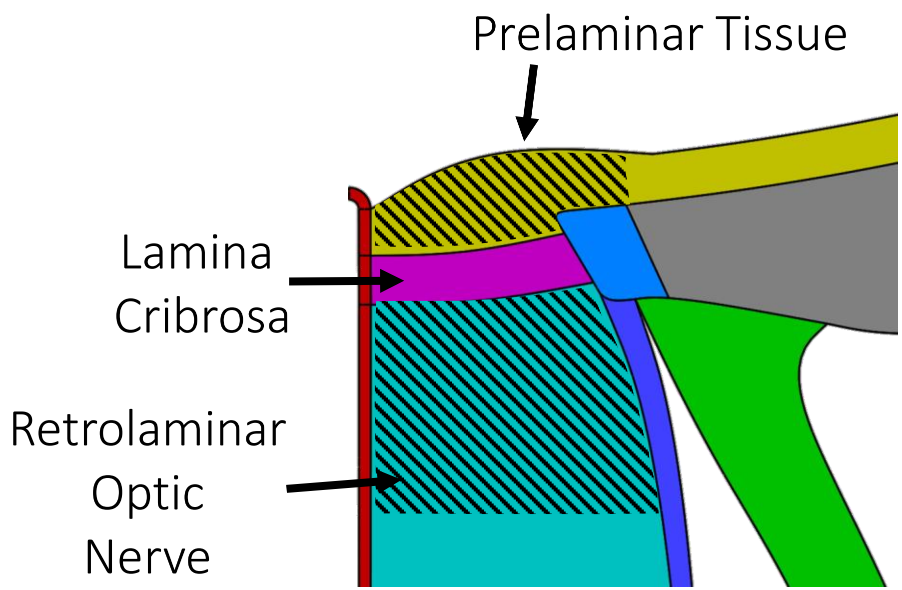
Outcome measures

- Strain (fractional tissue elongation) in all tissue regions
  - Strain is a tensor and can be decomposed into 3 primary components
    - First principal strain (stretch)
    - Second principal strain
    - Third principal strain (compression)
- Why do we care about strain?
    - Cells are mechanosensitive and alter their phenotype in response to mechanical strain

Finite Element Model

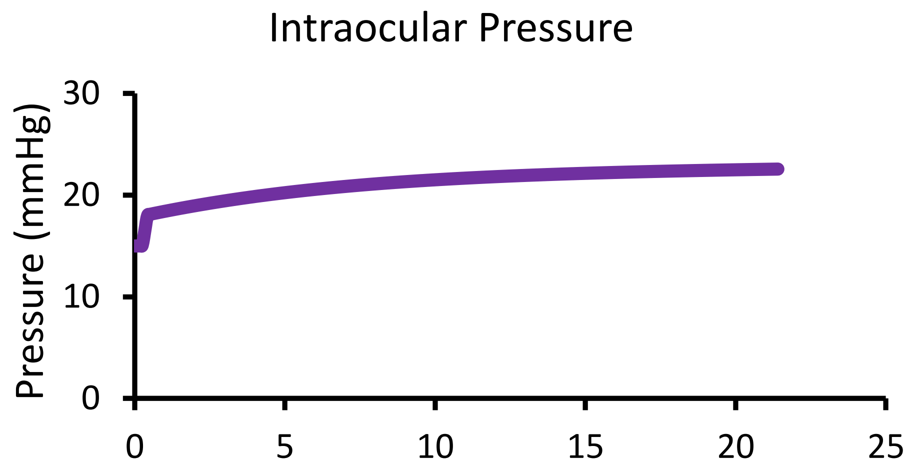
Primary outcome measures: peak tensile and compressive strains in the prelaminar tissue, lamina cribrosa and retrolaminar optic nerve

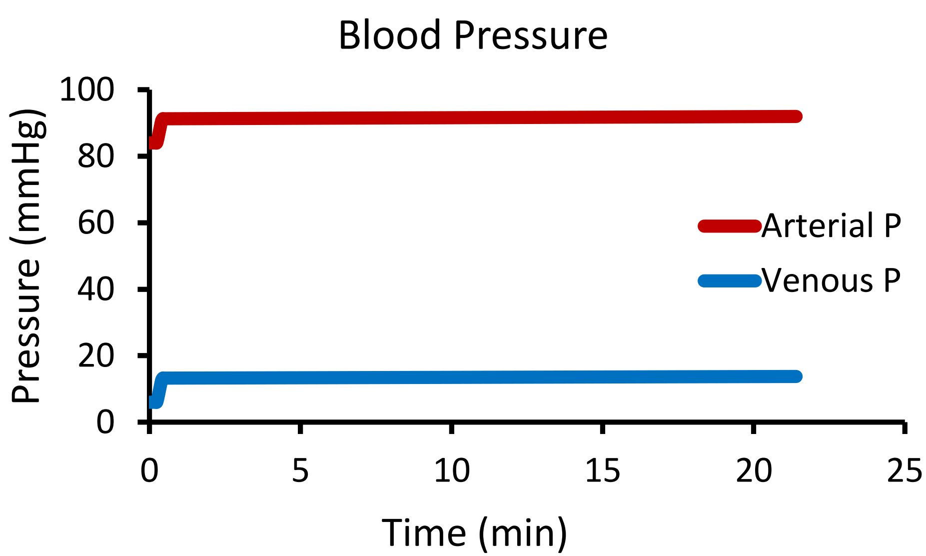
Regions of Interest:

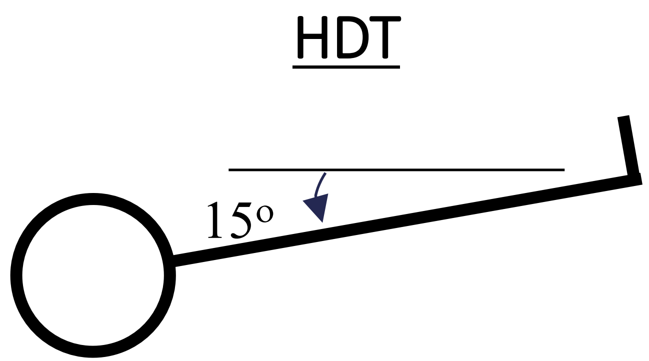


Results

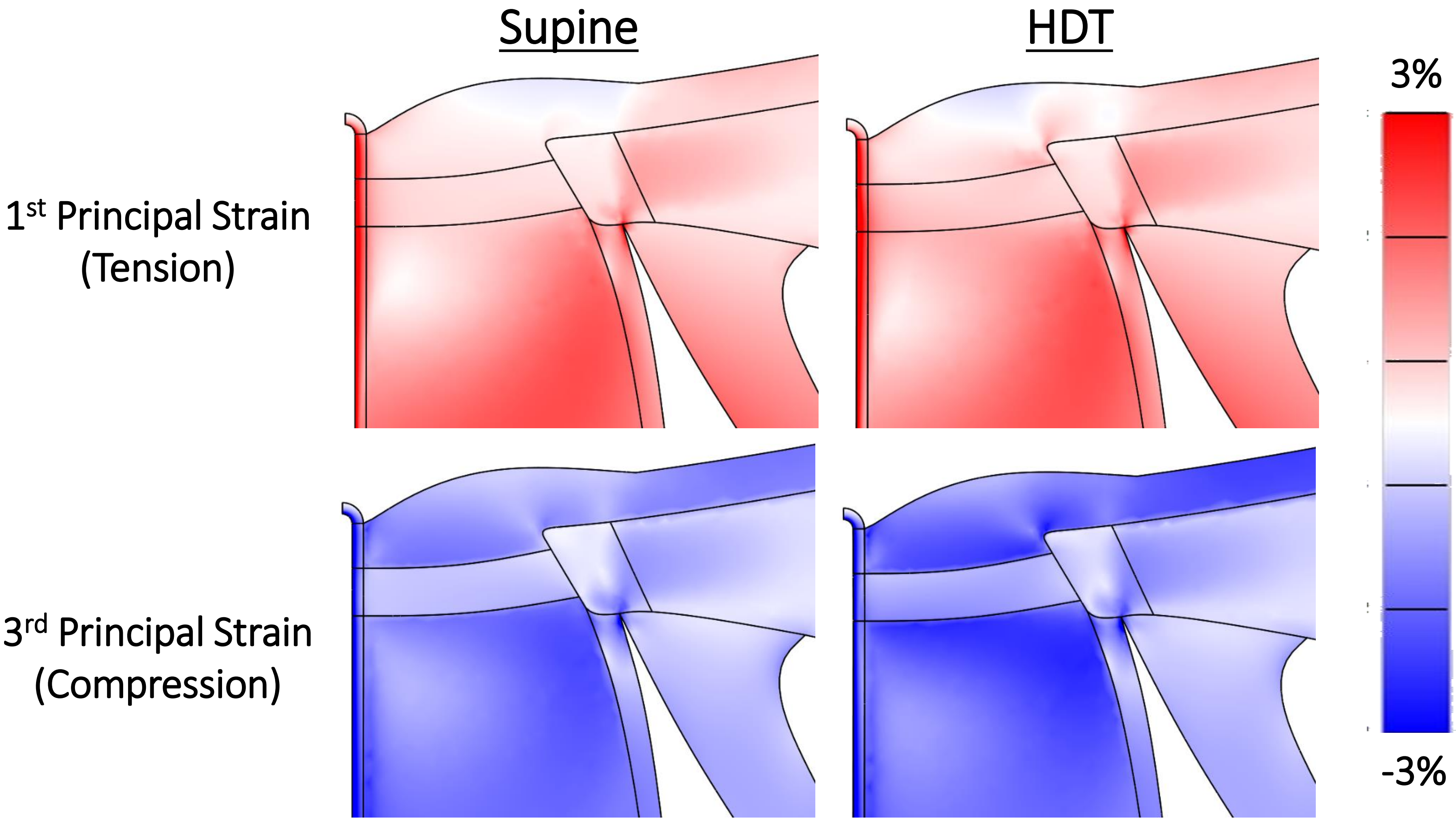
Pressures from Eye Model







Principal Strain Magnitudes



HDT on ONH Deformation

		Supine	HDT
Lamina Cribrosa	Tension	0.60%	0.93%
	Compression	-0.98%	-1.51%
Retrolaminar Optic Nerve	Tension	1.16%	1.39%
	Compression	-1.64%	-2.44%
Prelaminar Neural Tissue	Tension	0.77%	1.25%
	Compression	-1.75%	-2.69%

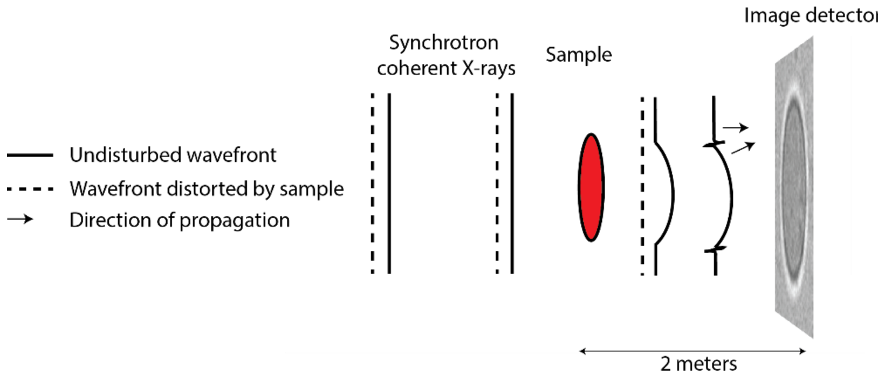
Summary

- Our integrated model approach predicts an increase in strains at the ONH after HDT
- These strains, if persistent, may induce a phenotypical change in ONH cells
- Future experimental work should examine how strains initiate a remodeling response in the optic nerve and optic nerve sheath

Experimental Effects of ICP on the Optic Nerve

Experiment Objective

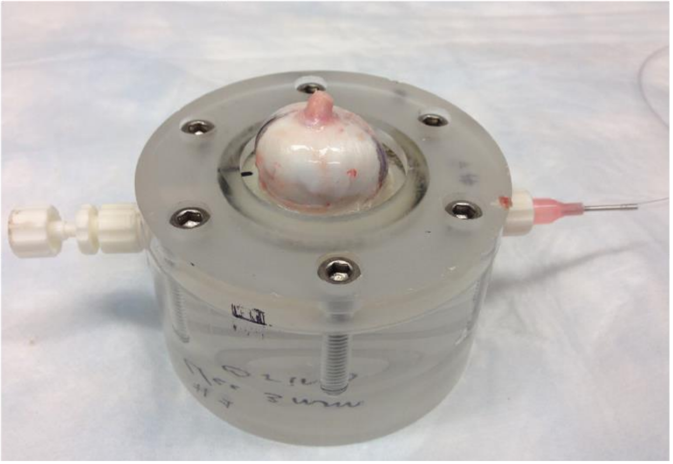
- Measure strain in the optic nerve due to elevations in ICP
  - Refraction of the X-ray by the sample
  - Tissues can be intact and untreated (no contrast agent required)

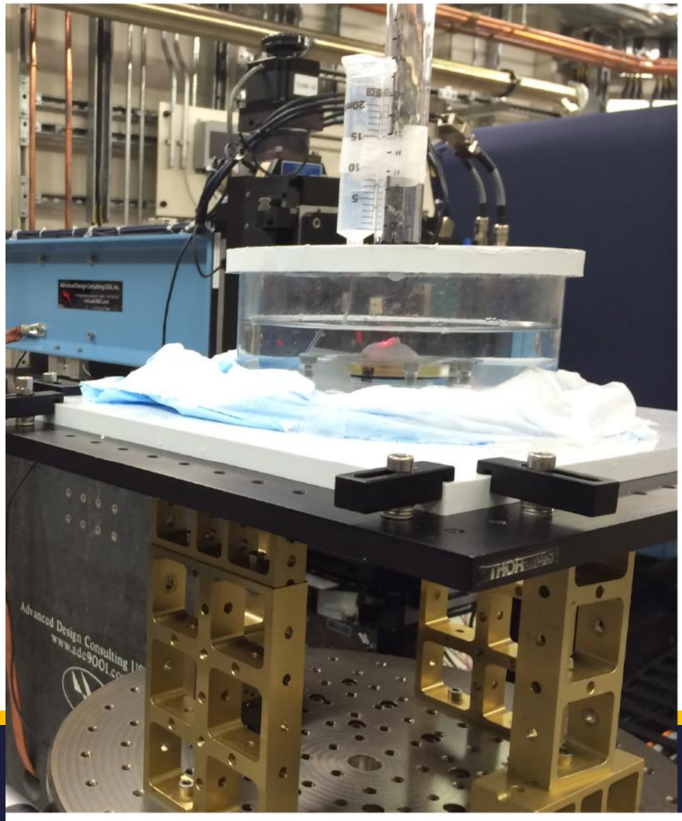


- However, for resolution of our small complex tissues requires X-rays with high spatial coherence

Experimental Design

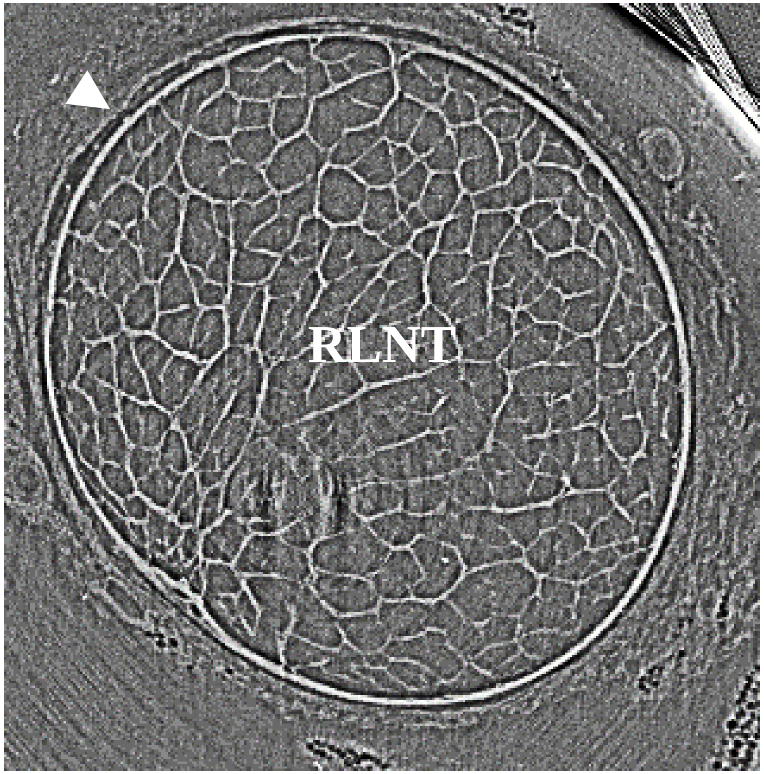
- 3 porcine eyes
  - Mirco-CT scans were acquired at an ICP = 4, 10, 20 & 30 mmHg
  - IOP was kept constant at 15 mmHg



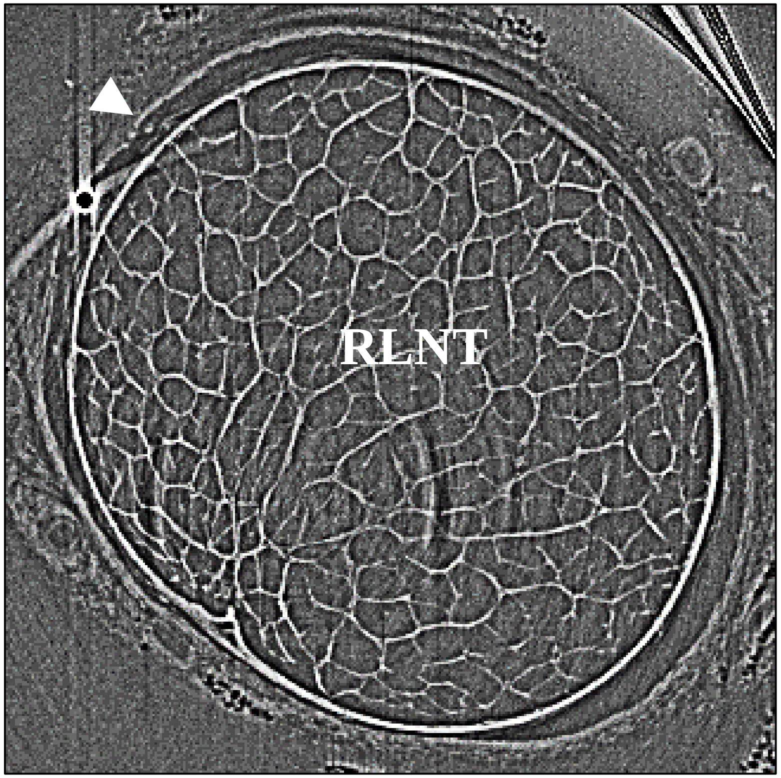


Phase-contrast micro-CT

Non-uniform expansion of the dura mater

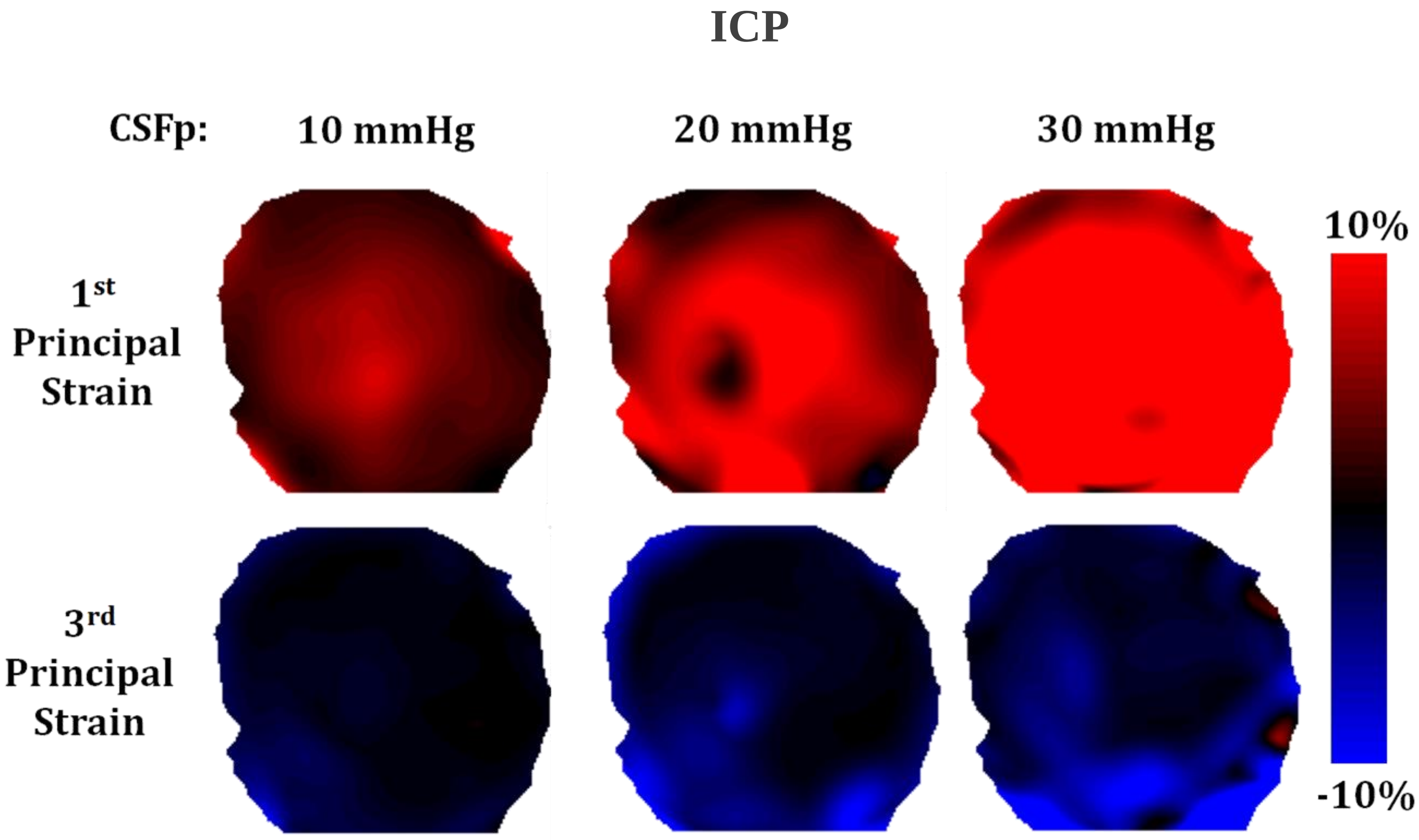


CSFp = 4 mmHg



CSFp = 30 mmHg

Optic Nerve Deformation

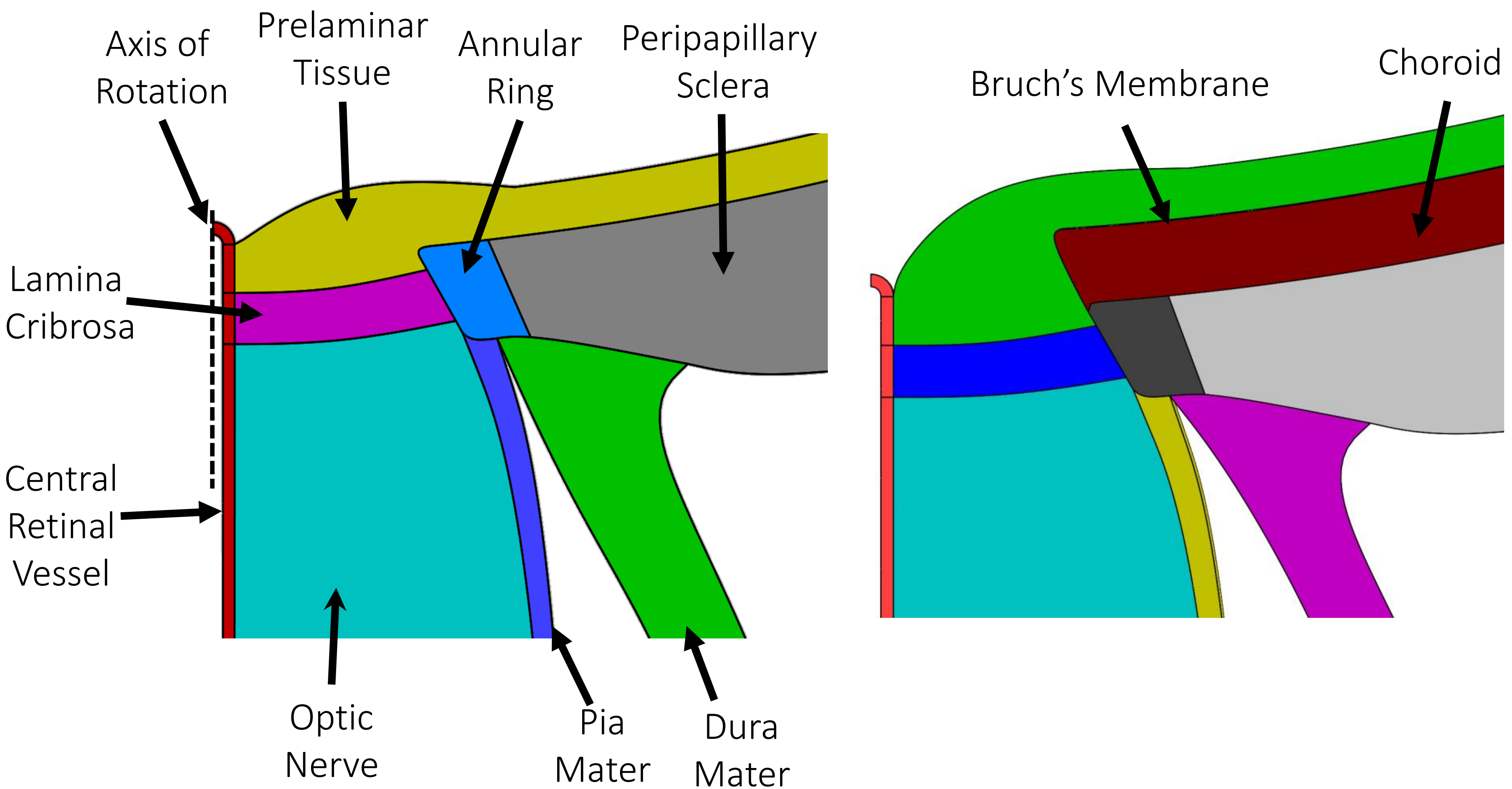


Experimental Work Summary

- Increased ICP directly elevated strains in the optic nerve
- Our experimental results agree with earlier finite element model work
  - The magnitude of strain was higher in experimental results

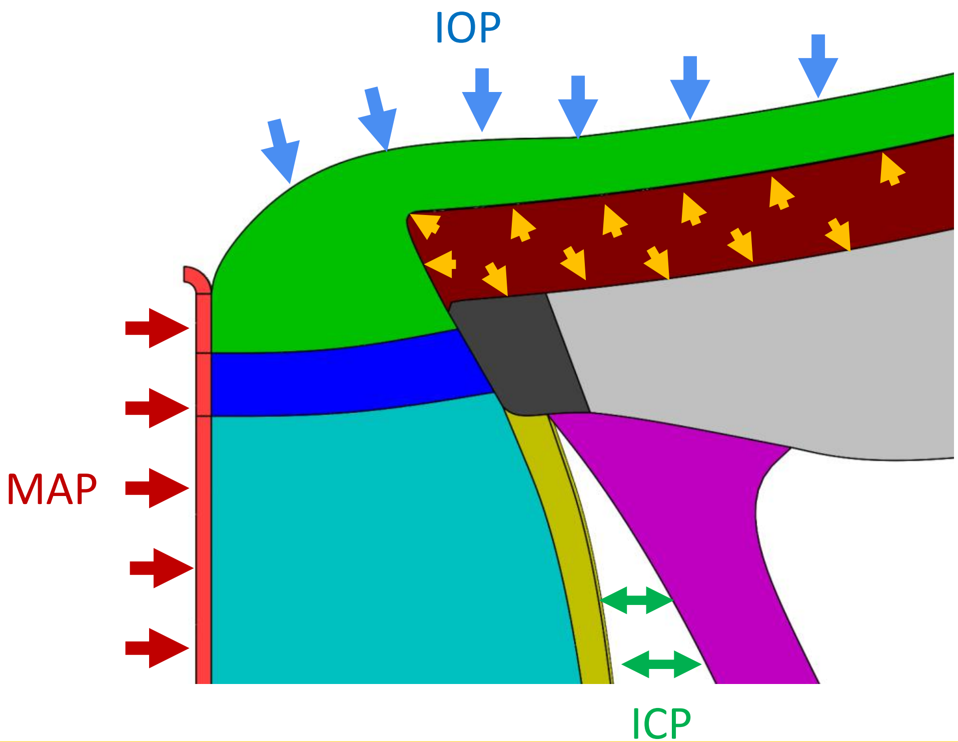
Ongoing Work

Additional FE Work

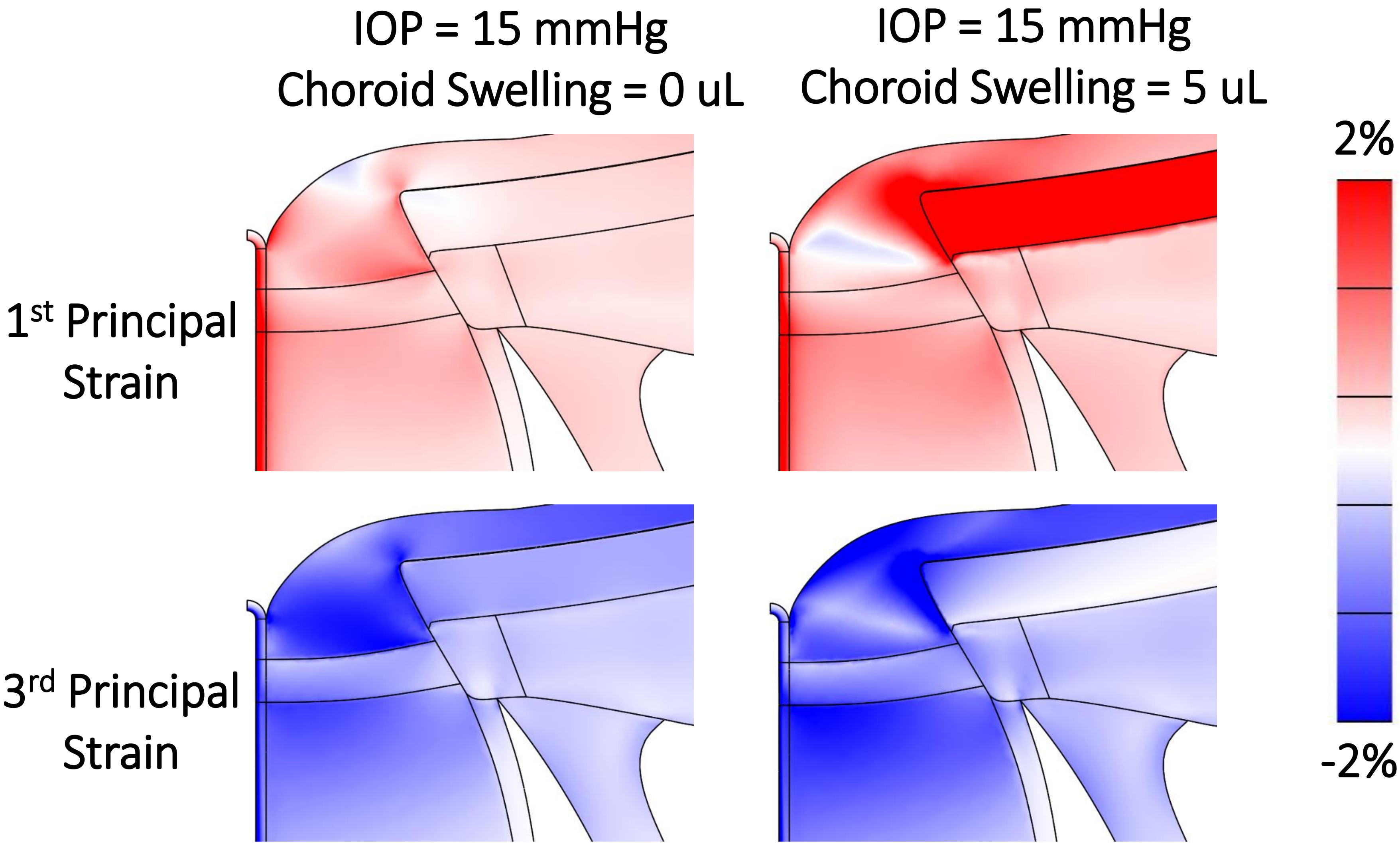


Simulate Choroidal Swelling

- Choroid modeled as a solid mixture to allow swelling
  - Linear-Elastic material (E = 0.3 MPa)
  - Apply uniform swelling (5 uL) to simulate volume change during cardiac cycle



Impact of Choroidal Swelling

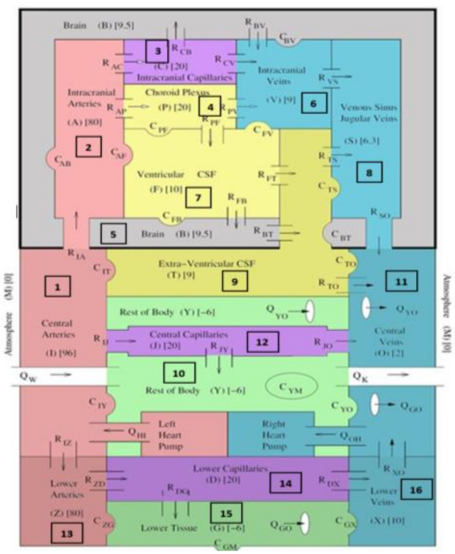


Advanced Model Integration

Latin Hypercube Sampling Inputs

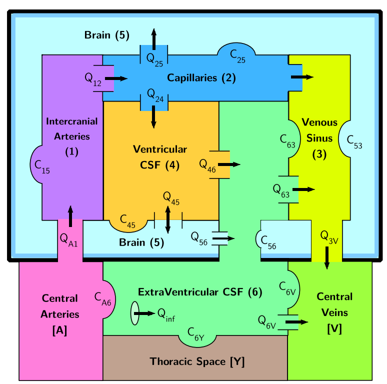
	Cardiovascular	Central Nervous	Eye Model	FEM
Run 1	$w_1....w_{42}$	$x_1....x_{17}$	$y_1....y_3$	$z_1....z_{20}$
Run 2	$w_1....w_{42}$	$x1....x_{17}$	$y_1....y_3$	$z_1....z_{20}$
Run N	$w_1....w_{42}$	$x_1....x_{17}$	$y_1....y_3$	$z_1....z_{20}$

16 Compartment Cardiovascular System



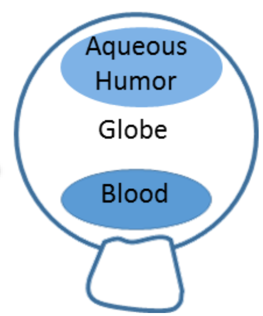
Blood Pressure

6 Compartment Central Nervous System

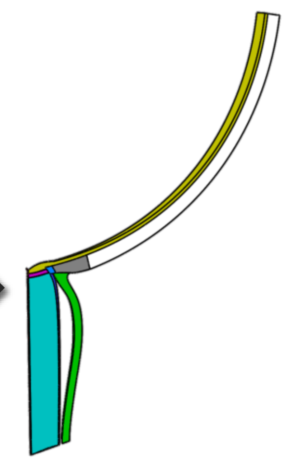


ICP

4 Compartment Eye



IOP



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